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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,248	11/13/2003	Jennie P. Mather	415072002300	1169

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,248	MATHER ET AL	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/28/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-12,15-22 and 26-51* is/are pending in the application.

4a) Of the above claim(s) *3-11,16-22 and 47-49* is/are withdrawn from consideration.

5)☒ Claim(s) *15,26,50 and 51* is/are allowed.

6)☒ Claim(s) *12 and 27-46* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/15/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 12/28/2007 is acknowledged. Claims 1, 13, 14, 23-25 were canceled. Claims 27-51 were added.

2. Claims 2-12, 15-22, 26-51 are pending. Claims 3-11, 16-22 and new claims 47-49, drawn to non-elected inventions, are withdrawn from consideration. Claims 2, 12, 15, and 26-46, 50 and 51 are examined on the merits.

Claim Rejections Withdrawn:

Claim Rejections - 35 USC § 112

3. The rejection of claims 2 and 15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of the amendment.

4. The rejection of claim 15 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, because of the lack of description of progeny for cell line deposited as ATCC No. PTA-4220, is withdrawn in view of the amendment.

5. The rejection of claims 1, 2, 12-14 and 23-25 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendments to the claims.

6. The rejection of claim 15 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not set forth in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention because the deposit requirement was not satisfied, is withdrawn in view of the submitted cop of the Deposit Receipt and the declaration by an officer of the assignee assuring the availability of the deposit as required under 37 C.F.R. 1.801-1.809.

7. The rejection of claims 1, 2, 12, 13, and 23-25 under 35 U.S.C. 102(b) as being anticipated by Smith (Smith, G.M. et al., Journal of Clinical Immunology, 17(6): 502-509, 1997; cited in the IDS) is withdrawn in view of the amendment to the claims.

8. The rejection of claims 1, 2, 12, 13, and 23-25 under 35 U.S.C. 102(b) as being anticipated by WO 97/35614 (published 2 October 1997) is withdrawn in view of the amendment to the claims.

9. The rejection of claims 1, 23 and 25 under 35 U.S.C. 102(b) as being anticipated by Ianelli (Ianelli, C.J. et al, The Journal of Immunology, 159: 3910-3920, 1997) is withdrawn in view of the amendment.

Claim Rejections Maintained and New Grounds of Rejection:

10. Claims 30-32 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel

the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 30-32 are objected to because they are dependent from a claim to a particular antibody species, that of an antibody that is produced by a host cell with ATCC deposit number PTA-4220, but they are drawn to non-antibody products. Claims 30-32 are drawn to heavy chains and light chains, which are products that are not within the scope of claim 26, from which these claims are dependent.

11. Claim 2 is objected to because it is drawn to an antibody of claim 52 and there is no claim 52.

12. Claim 34 is objected to because there is a period after "26" instead of a comma.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 27-29, 33-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27-29, 33, 37 and 40 are indefinite because of the phrase "or retains" with respect to the binding specificity. The antibody either has or has not the binding specificity of the PIP antibody. It is not clear what limitation is intended by the inclusion of the phrase "or retains".

Claim 27 is indefinite because of the phrase "said antibody". There are two antibodies referred to, the chimeric antibody and the human antibody.

Claim 28 is indefinite because of the phrase "said antibody". There are two antibodies referred to, the humanized antibody and the human antibody.

Claims 27-29, 33, 37, 40 are indefinite because the indefinite article is used instead of the definite article. For example, in claims 27, the claim should read: A chimeric antibody comprising the variable regions of *the* light chain and *the* heavy chain of the antibody PIP of claim 26 and constant regions of *the* light chain and *the* heavy chain of a human antibody, ...

14. Claims 30-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific monoclonal antibody, PIP, which is secreted by the hybridoma cell line ATCC No. PTA-4220, does not reasonably provide enablement for any antibody that binds to "PIPA", and antigen that is characterized only by name and as a GPI-linked cell surface protein having a molecular weight 45-50 kD, or for a heavy chain of the antibody PIP, for a light chain of the antibody PIP, or for a light chain comprising the three CDRs of a heavy chain of the antibody PIP. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification teaches one example of an antibody that binds to PIPA, which is an antigen characterized only by name and as a GPI-linked cell surface protein having a molecular weight of 45-50 kD. While the specification does provide the amino acid sequences of the variable domains of the heavy and light chains, these structures are not the same as the structures

of the particular heavy and light chains that are specific to antibody PIP, because both the heavy and light chains of an antibody include constant regions in addition to variable domain regions. Therefore, the specification does not actually provide the structures of the isolated heavy and light chains of the antibody PIP. However, the more important question concerning claims 30-32 is the use of the claimed heavy and light chains.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

It is not clear from the specification, what use is contemplated for a heavy or a light chain of the antibody PIP as isolated polypeptides. One possibility is that each of these chains may be used in the construction of other antibodies. However, undue experimentation would be required by one of skill in the art to use the inventions of claims 30-32 to make antibodies that bind to PIPA, which is an uncharacterized antigen.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which heavy and light chain variable regions consists of three CDRs that provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity that is characteristic of a given

antibody. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences, which maintain the required conformation of the CDRs, are required in order to produce a protein having antigen-binding function; and further, that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light chain variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff (Proc. Natl. Acad. Sci. USA, 79: 1979, 1982). Rudikoff teaches that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. Therefore, it is unlikely that antibodies formed from pairing a heavy chain or a light chain from the specific antibody PIP with another, undescribed heavy or light chain, will have the required binding function, especially in light of the fact that the antigen is uncharacterized. Additionally, isolated heavy or light chains contain less that the full complement of CDRs present in the parent antibody, also making it unlikely that either the heavy chain or the light chains as claimed will have the requisite binding specificity or affinity.

The specification provides no direction or guidance regarding how to produce the humanized antibodies as broadly defined by the claims, because the specification fails to teach how to make antibodies that do not contain all of the CDRs present in the parent antibodies. The relationship between structure and function in the protein and antibody arts is highly unpredictable. Therefore, one of skill in the art would have to engage in undue experimentation to practice the full scope of the claimed inventions. This experimentation would be undue

experimentation because the antigen to which the parent antibody binds is uncharacterized, and it is not clear how one would use the claimed heavy and light chains.

15. Claim 12 remains rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions comprising the specific antibody secreted by the hybidoma, ATCC No. PTA-4220, wherein the antibody is conjugated or bound to a therapeutic agent or toxin, does not reasonably provide enablement for pharmaceutical composition comprising any antibody to PIPA or comprising the specific antibody secreted by the hybridoma ATCC No. PTA-4220, wherein the specific antibody is not conjugated or bound to a therapeutic agent or toxin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is that the intended use of the full scope of the claimed pharmaceutical compositions is not enabled by the disclosure of the specification.

Applicants' amendment to claim 12 fails to obviate the rejection of record, because the therapeutic moiety is not conjugated to the antibody. Therefore, for the reasons stated in the previous Office action, the specification is not enabling the pharmaceutical composition of claim 12.

Conclusion

Claims 15, 26, 50 and 51 are allowable. Claims 12, 27-46 are rejected. Claim 2 is objected to.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official

Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
April 3, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER